UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/827,054	04/19/2004	David R. Elmaleh	62041(51588)	2370

71284 7590 02/13/2008

EWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
02/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/827,054	ELMALEH ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,32-54,118,119,122-125 and 147-153* is/are pending in the application.

4a) Of the above claim(s) *5,6,8,10,14-16,32-43,48,49,51,53,118,122 and 124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,9,11-13,17,44-47,50,52,54,119,123,125 and 147-151* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/23/07 has been entered.

2. The declaration under 37 CFR 1.132 filed 11/23/07 is insufficient to overcome the rejection of claims 1-4,7,9,11-13,17,44-47,50,52,54,119,123,125 and 147-151 based upon the rejection under 35 U.S.C. 103(a) as being unpatentable over Elmaleh (WO97/19705) in view of Knust et al. (US 4,323,547) and Elmaleh et al. (US 4,524,059) as set forth in the last Office action because: the declaration provided data showing the improved uptake of the [^{18}F]FCPHA and enhanced heart to tissue/blood ratio but it is not correct to disregard the fact that Elmaleh et al. (US 4,524,059) discloses that a substituent (i.e. methyl) at the C3 position along the fatty acid chain analog is necessary to lower the rate of in vivo beta-oxidation and causes the analog to be metabolically trapped in the heart tissue by permitting the first beta-oxidation step during which the carbon atom to which the substituent is bonded is beta to the carboxyl carbon to occur, while preventing the cleaving off from the analog of the two carbon atoms to the right of the carbon atom to which the substituent is bonded (column 1, lines 31-51). Elmaleh

(WO97/19705) discloses a fatty acid analog imaging agent containing a radionuclide in spatial proximity to the stereocenter (cyclopropyl substituent) along the carbon chain at the C2-C3 position of the fatty acid chain. The fatty acid analog imaging agent of Elmaleh (WO97/19705) allows for imaging the cardiovascular (heart) tissue. Both disclosures of Elmaleh et al. are drawn to the same utility, such as for uptake and imaging of the heart tissue. In combination (Elmaleh et al. (US 4,524,059) and Elmaleh (WO97/19705)), it would be obvious to one ordinarily skilled in the art to have a substituent at the C3 position (i.e. methyl or at least one carbon of the cyclopropyl ring) of the fatty acid chain of the analog. It would be obvious that the cyclopropyl group must either be at the C2-C3 position or it would be obvious to provide/try a C3-C4 cyclopropyl substituent where one of the carbon atoms of the ring (substituent) must necessarily be at the C3 position. It would be obvious to try either C2-C3 or C3-C4 cyclopropyl as long as one of the carbons of the cyclopropyl is provided at the C3 position.

Claims and Previous Rejection Status

3. Claims 1-17,32-54,118,119,122-125 and 147-153 are pending in the application. Claims 5,6,8,10,14-16,32-43,48,49,51,53,118,122 and 124 are withdrawn. Claims 18-31,55-117,120,121 and 126-146 were canceled and claims 152 and 153 were newly added in the amendment filed 11/23/07.

4. The rejection under 35 U.S.C. 103(a) as being unpatentable over Elmaleh (WO97/19705) in view of Knust et al. (US 4,323,547) and Elmaleh et al. (US 4,524,059) is maintained (see below).

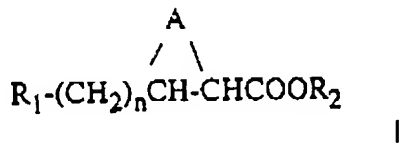
Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4,7,9,11-13,17,44-47,50,52,54,119,123,125 and 147-151 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elmaleh (WO97/19705) in view of Knust et al. (US 4,323,547) and Elmaleh et al. (US 4,524,059).

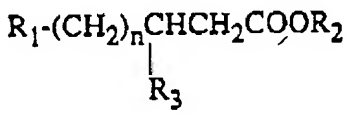
7. Elmaleh (WO97/19705) discloses a fatty acid imaging agent containing a radionuclide in spatial proximity to the stereocenter (cyclopropyl substituent) along the carbon chain of the formula I (below) (p4, lines 19-30).



I

R_1 may be hydrogen, fluorine, aryl or substituted aryl, vinyl, substituted vinyl, etc. which encompasses those of the instant claims. R_2 may be hydrogen, alkyl, amine, etc., A is selected from the group methylene, oxygen, sulfur, nitrogen and n is greater than 10, these limitations also encompass those of the instant claims. The A (methylene)

substituent is bonded to the fatty acid backbone chain at the C2,C3 positions. Elmaleh also discloses a fatty acid imaging agent containing a radionuclide of the formula II containing a substituent at the C3, position (below) (p4, lines 7-18).



II

R_1 may be hydrogen, fluorine, iodoaryl, iodoallyl, etc. which encompasses those of the instant claims. R_2 may be hydrogen, alkyl, amine, etc., R_3 is selected from the group halide, hydrogen, etc. and n is greater than 12, these limitations also encompass those of the instant claims. Administration of these radioactively labeled fatty acid imaging agents (above) allows for imaging the cardiovascular (heart) tissue and detecting the accumulation of the imaging agent in the cardiovascular (heart) tissue or a heart lesion by PET (p5, lines 14-24; p16, line 3). The detection of a heart tumor indicates a region of enhanced metabolism at the site of the tumor (p19, lines 4-8). The radionuclides suitable for use in PET are positron emitters; ^{123}I, ^{18}F, etc. which may be covalently bonded to an atom of the fatty acid moiety (p16, lines 3-6). Elmaleh (WO97/19705) does not disclose the substitution of the cyclopropyl ring at the C3-C4 position of the fatty acid carbon chain or does not explicitly disclose that the fatty acid chain is heptadecanoic acid.

8. Knust et al. (US 4,323,547) discloses fatty acids labeled with radioactive isotopes and the methods of making and using these analogs, such as the method of investigating the kinetics of heart muscle exchange, i.e. myocardial metabolism (column 1, lines 6-10). It is discloses that the pickup of a ϖ-F-fatty acid is greater than that of a

ϖ-iodo-fatty acid: with ϖ-^{18}F-heptadecanoic acid a rapid pickup of a maximum of about 40%/g heart is found with heart muscle (column 1, lines 38-42). This advantageous maximum pickup is accompanied by a delayed elimination as is desired for radiographic studies which makes these positron emitting ϖ-^{18}F- labeled fatty acids especially useful for myocardial investigations (column 1, lines 43-48). Centrally labeled or midsubstituted ^{18}F- labeled fatty acids having 10-20 carbon atoms in the carbon chain are also effective in the investigations of the kinetics of heart muscle exchange but known α-^{18}F- labeled fatty acids are less effective than the ϖ-^{18}F- labeled fatty acids with regards to maximum enrichment in the myocardium (column 2, lines 6-10 and 25-36).

9. Elmaleh et al. (US 4,524,059) discloses radioactively labeled fatty acid analogs (having a chain of six or more carbon atoms) that that are substituted at the C3 carbon atom of the fatty acid backbone chain, causing the analog to be metabolically trapped in the heart tissue and permitting the occurrence of the first beta-oxidation step in which the carbon atom to which the substituent is bonded is beta to the carbonyl carbon atom. The substituent at the C3 position lowers the rate of the in vivo beta-oxidation of the analog (claims 1-6). The chain length of 12-20 carbon atoms is optimal for selective uptake by myocardial tissue (column 2, lines 65-67) and the substituent at the C3 position of the analog traps the analog in the metabolizing tissue and inactivates the beta-hydroxyacyl dehydrogenase to which the analog (column 9, lines 3-17). The radioisotopes of the disclosure are halogen isotopes that may be placed at any position on the chain (column 10, lines 10-15).

10. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize a ^{18}F-heptadecanoic acid as disclosed by Knust et al. (US 4,323,547) for the carbon backbone chain of the fatty acid disclosed by Elmaleh (WO97/19705) to incorporate the advantageous properties of the ^{18}F-heptadecanoic acid, such as the maximum pickup/incorporation into heart of tumor tissue and delayed release which has not been found to be attainable with various known preparations of other radioactively labeled fatty acid analog, such as ^{123}I-substituted fatty acid analogs. Elmaleh et al. (US 4,524,059) also discloses that a chain length of 12-20 carbon atoms is optimal for selective uptake by myocardial tissue. All of the references of Elmaleh (WO97/19705), Elmaleh et al. (US 4,524,059) and Knust et al. (US 4,323,547) disclose various points of attachment of the radioisotope (^{18}F) along the carbon chain of the fatty acid. For example, radionuclides suitable for use in PET are positron emitters; ^{123}I, ^{18}F, etc. which may be covalently bonded to an atom of the fatty acid moiety analog centrally labeled or midsubstituted (Elmaleh WO97/19705) and centrally labeled or midsubstituted ^{18}F-labeled fatty acids having 10-20 carbon atoms in the carbon chain were examined by Knust et al. It is also very obvious to one ordinarily skilled in the art to vary a substituent position along the chain of a molecule to compare the chemical and physical properties of such analogs. Elmaleh et al. (US 4,524,059) discloses that a substituent (i.e. methyl) at the C3 position along the fatty acid chain analog is necessary to lower the rate of in vivo beta-oxidation and causes the analog to be metabolically trapped in the heart tissue by permitting the first beta-oxidation step during which the carbon atom to which the substituent is bonded is beta to the carboxyl carbon to occur, while preventing the

cleaving off from the analog of the two carbon atoms to the right of the carbon atom to which the substituent is bonded (column 1, lines 31-51). Both disclosures of Elmaleh et al. are drawn to the same utility, such as for uptake and imaging of the heart tissue. One would have a reasonable expectation of success for specific uptake and metabolic trapping of the product of the combined disclosures into heart tissue when a cyclopropyl group at the C3 position of a ^{18}F-heptadecanoic acid by allowing for first beta-oxidation step. The combination of Elmaleh et al. (US 4,524,059) and Elmaleh (WO97/19705), provides the teaching of a C3 substituent (i.e. methyl or at least one carbon of the cyclopropyl ring) substituted ^{18}F-heptadecanoic acid where the ^{18}F may be located at any point along the heptadecanoic chain, including C9. Where one of the carbon atoms of the ring (substituent) must necessarily be at the C3 position, it would be obvious that the cyclopropyl group must either be at the C2-C3 position or it would be obvious to provide/try a C3-C4 cyclopropyl substituent. It would be obvious to try either C2-C3 or C3-C4 cyclopropyl as long as one of the carbons of the cyclopropyl is provided at the C3 position.

Response to Arguments

Applicant asserts that for the reasons described in the papers filed 3/12/07 and 7/20/07, none of the references cited, alone or in combination renders obvious the pending claims.

The examiner therefore also draws attention to the response to the arguments provided in papers filed 3/12/07 and 7/20/07 for each assertion.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
January 14, 2008

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER